

- (c) a selectable marker located between the first and second polynucleotide sequences; and
  - (d) wherein where said targeting construct is introduced into a murine embryonic stem cell and homologously recombines with the stefin homolog gene, said homologous recombination disrupts the stefin homolog gene.
- 2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
- 3. (Twice Amended) A method of producing a targeting construct, the method comprising:
  - (a) providing a first polynucleotide sequence homologous to at least a first portion of an endogenous murine stefin homolog gene comprising SEQ ID NO: 1;
  - (b) providing a second polynucleotide sequence homologous to at least a second portion of the stefin homolog gene;
  - (c) providing a selectable marker located between the first and second polynucleotide sequences; and
  - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
- 4. (Twice Amended) A method of producing a targeting construct, the method comprising:
  - (a) providing a polynucleotide comprising a first sequence homologous to a first region of an endogenous murine stefin homolog gene comprising SEQ ID NO: 1 and a second sequence homologous to a second region of the stefin homolog gene;
  - (b) inserting a positive selection marker between the first and second sequences to form the targeting construct; and
  - (c) wherein where said targeting construct is introduced into a murine embryonic stem cell and homologously recombines with the stefin homolog gene, said homologous recombination disrupts the stefin homolog gene.
- 5. (Twice Amended) A murine embryonic stem cell comprising a genome

comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1; wherein said cell, when introduced into a blastocyst, produces a transgenic mouse comprising a genome having a disruption in the stefin homolog gene, wherein where the mouse is homozygous for the disruption, the mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of increased activity and a neuropsychological disorder.

Claim 6 is canceled.

Claim 7 is canceled.

8. (Twice Amended) A transgenic mouse comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1; wherein where the disruption is homozygous, the transgenic mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of increased activity and a neuropsychological disorder.
9. (Amended) A cell derived from the transgenic mouse of claim 8.
10. (Twice Amended) A method of producing a transgenic mouse comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1, the method comprising:
  - (a) introducing the targeting construct of claim 1 into a murine embryonic stem cell;
  - (b) introducing the cell into a blastocyst;
  - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
  - (d) breeding the chimeric mouse to produce the transgenic mouse.
11. (Twice Amended) A method of identifying an agent that ameliorates a phenotype associated with a disruption in a stefin homolog gene, the method comprising:
  - (a) providing the transgenic mouse of claim 8;
  - (b) administering an agent to the mouse; and
  - (c) determining whether the phenotype is ameliorated.

Claim 12 has been canceled.

13. (Twice Amended) A method of identifying an agent that ameliorates a phenotype

associated with a disruption in a stefin homolog gene, the method comprising:

- (a) providing the cell of claim 5;
- (b) contacting the cell with an agent; and
- (c) determining whether the phenotype, produced by the insertion of the cell into the blastocyst according to claim 5, is ameliorated.

Claim 14 has been canceled.

Claim 15 has been canceled.

Claim 16 has been canceled.

Claim 17 has been canceled.

Claim 18 has been canceled.

Claim 19 has been canceled.

- 20. (Amended) The transgenic mouse of claim 8, wherein the increased activity is characterized by increased velocity of movement in an open-field test.
- 21. (Amended) The transgenic mouse of claim 8, wherein the neuropsychological disorder comprises a decreased propensity for despair or depression.
- 22. (Amended) The transgenic mouse of claim 21, wherein the decreased propensity for despair or depression is characterized by a decreased amount of time spent immobile when tail-suspended.
- 23. (Amended) The transgenic mouse of claim 8, wherein the neuropsychological disorder comprises a stimulus-processing deficit.
- 24. (Amended) The transgenic mouse of claim 23, wherein the stimulus-processing deficit is characterized by decreased pre-pulse inhibition.
- 25. (Amended) The transgenic mouse of claim 24, wherein the decreased pre-pulse inhibition is consistent with schizophrenic behavior.

Claim 26 has been canceled.

Claim 27 has been canceled.

Claim 28 has been canceled.

Claim 29 has been canceled.

Claim 30 has been canceled.

Claim 31 has been canceled.